Remarks

Claims 1, 2, and 117-127 were pending. Claims 117, 119, 120, 122, 124 and 127 have been canceled. Applicants have amended claims 1, 2, 118, 121, 123, 125 and 126. New claims 128-135 were added. Therefore, claims 1, 2, 118, 121, 123, 125, 126 and 128-135 are now pending.

Claim 1 has been amended to restrict the claim to diagnosis of cancer, and to restrict the nucleic acids detected to those shown in the specification not to be expressed in any normal tissue (SOX1, SOX3 and SOX21). Claim 2 has been amended to restrict the claim to certain agents encoded by certain nucleic acid molecules, or which recognize the expression products of certain nucleic acid molecules. New claim 128 and dependent claims 129-131 were added to cover specifically the SOX2 subject matter deleted from claims 1 and 2. New claim 132 and dependent claims 133-135 were added to cover specifically the ZIC2 subject matter deleted from claims 1 and 2. No new matter has been added.

Applicants note that in response to the restriction requirement mailed on April 24, 2001, Applicants elected invention I, claims 1 and 2, with the understanding that the restriction requirement with respect to linked inventions (inventions I, II and III) will be withdrawn upon the allowance of linking claims 1 and 2. Therefore, Applicants reserve the right to add claims to linked inventions II and III upon allowance of claims 1 and 2 (and/or new claims 128, 131, 132, and 135, the subject matter of which was split from claims 1 and 2 for clarity of claiming).

Rejections Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 1, 2, 117-127 under 35 U.S.C. 112, first paragraph as not enabled by the specification. Applicants have amended several of the claims and respectfully request reconsideration.

The claims have been amended in several ways to overcome the enablement rejection. First, the claims now recite specifically the disorder that is diagnosed by the claimed methods, cancer. Second, claims 1 and 2 have been amended to recite only the three nucleic acid sequences that are not expressed in any normal tissues as disclosed in the specification (SOX1, SOX3 and SOX21). The other two nucleic acids that were recited in claim 1, SOX2 and ZIC2, are now recited in individual claims (claims 128 and 132, respectively). The claims that recite

SOX2 and ZIC2 have excluded from them the particular normal tissues in which SOX2 or ZIC2 are expressed. Thus the Examiner's notation regarding levels of expression (Office Action at page 7) does not apply to the claims as amended.

The Examiner asserted that undue experimentation would be required to practice the invention as claimed. Applicants respectfully assert that even if true (which Applicants do not agree with), the claims as presently amended would not require undue experimentation because the claims are limited to detection of cancer, and are limited to application in tissues in which the specific genes are not normally expressed. Moreover, the methods that one of ordinary skill in the art would need to practice the invention are (1) well known in the art, (2) routinely practiced by one of ordinary skill in the art, and (3) described in the specification to provide the skilled artisan with sufficient guidance to practice the invention. Thus, any experimentation required to practice the invention would be routine for the person of skill in the art, and thus not undue. Considering the high level of skill in the relevant art, Applicants maintain that the claims for methods of diagnosing cancer, as amended, would not require undue experimentation.

Rejections Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 1, 2 and 117-127 under 35 U.S.C. 112, second paragraph as indefinite.

Claim 1 was rejected as unclear for the recitation of "an agent that binds under stringent hybridization conditions to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof ..." in lines 4-5 of the claim. The Examiner stated that it is unclear how an agent would bind under stringent hybridization conditions to an expression product or fragment of the expression product, as the expression product could be, for example, a peptide. Claim 1 has been amended to recite that the agent binds specifically to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof

The Examiner further rejected claim 1 as unclear as to what codes for a "cancer-associated antigen precursor" - the nucleic acid which hybridize to the sequence, or the nucleic acid sequences recited by SEQ ID NO. Applicants have amended claim 1 to clarify this point by

reciting that the nucleic acid molecules that encodes the cancer- associated antigen precursor are those which hybridize to the recited sequences.

The Examiner also asserted that claim 1 is further unclear because it recites (1) and then followed by (b) and (c). Applicants have amended claim 1 to follow the Examiner's suggestion that (1) be written to recite (a).

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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x01/17/03

MARKED-UP CLAIMS

1. (thrice amended) A method of diagnosing cancer [a disorder characterized by expression of a human cancer associated antigen precursor coded for by a nucleic acid molecule], comprising:

contacting a biological sample isolated from a subject with an agent that specifically binds [under stringent hybridization conditions] to [the] a nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule is selected from the group consisting of [(1)] (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NOs:[3-17] 4, 11 and 12, [and which] wherein the hybridizing nucleic acid molecules code for a cancer associated antigen precursor, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and (c) complements of (a) or (b), and

determining the presence or level of interaction between the agent and the nucleic acid molecule or the expression product as [a determination of] an indication that the subject has the cancer [disorder].

2. (amended) The method of claim 1, wherein the agent is selected from the group consisting of

(a) a nucleic acid molecule comprising [NA group 1 nucleic acid molecules] any one of SEQ ID NOs:4, 11 and 12 or a fragment thereof,

(b) [a nucleic acid molecule comprising NA group 3 nucleic acid molecules or a fragment thereof,

(c) a nucleic acid molecule comprising NA group 5 nucleic acid molecules or a fragment thereof,

(d)] an antibody that binds to an expression product of [NA group 1 nucleic acids] any one of SEQ ID NOs:4, 11 and 12, and

[(e) an antibody that binds to an expression product of NA group 3 nucleic acids,

(f) an antibody that binds to an expression product of NA group 5 nucleic acids,

(g)][(c)] an agent that binds to a complex of an HLA molecule and a fragment of an expression product of [a NA group 1 nucleic acid] any one of SEQ ID NOs:4, 11 and 12.[,

(h) an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 3 nucleic acid, and

(i) an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 5 nucleic acid.]

118. (amended) The method of claim 1, wherein the cancer [disorder] is [selected from the group consisting of] small cell lung cancer[, non-small cell lung cancer, melanoma, colon cancer, breast cancer, head and neck cancer, transitional cancer, leiomyosarcoma and synovial sarcoma].

121. (amended) The method of claim 1, wherein the nucleic acid molecule is selected from the group consisting of [SOX2 (SEQ ID NO:3),] SOX1 (SEQ ID NO:4), [ZIC2 (SEQ ID NO:5),] SOX3 (SEQ ID NO:11) and SOX21 (SEQ ID NO:12).

123. (amended) The method of claim [1] 121, wherein the nucleic acid molecule is SOX1 (SEQ ID NO:4).

125. (amended) The method of claim [1] 121, wherein the nucleic acid molecule is SOX3 (SEQ ID NO:11).

126. (amended) The method of claim [1] 121, wherein the nucleic acid molecule is SOX21 (SEQ ID NO:12).